

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number  
**WO 03/086416 A1**

(51) International Patent Classification<sup>7</sup>: A61K 31/70, C12N 15/11

(21) International Application Number: PCT/CA03/00480

(22) International Filing Date: 8 April 2003 (08.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
2,380,970 8 April 2002 (08.04.2002) CA

(71) Applicant (for all designated States except US): SARISSA INC. [CA/CA]; 121 Timber Drive, London, Ontario N6K 4A2 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): KOROPATNICK, D., James [CA/CA]; c/o London Regional Cancer Center, 790 Commissioners Road East, London, Ontario N6A 4L6 (CA). VINCENT, Mark, D. [CA/CA]; c/o London Regional Cancer Center, 790 Commissioners Road East, London, Ontario N6A 4L6 (CA).

(74) Agent: MBM & CO.; P.O. Box 809, Station B, Ottawa, Ontario K1P 5P9 (CA).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



WO 03/086416 A1

(54) Title: COMBINATIONS OF ANTISENSE OLIGONUCLEOTIDES DIRECTED AGAINST THYMIDYLATE SYNTHASE MRNA AND USES THEREOF

(57) **Abstract:** Effective combinations of antisense oligonucleotides directed against thymidylate synthase mRNA are provided for use in cancer therapies. Combinations of antisense oligonucleotides have enhanced activity compared to the activity of the individual antisense oligonucleotides when used alone. The combinations may be used in conjunction with one or more chemotherapeutic agents to enhance the effects of the chemotherapeutic(s). Such antisense oligonucleotide combinations constitute improved antisense therapies with application to a variety of cancers or proliferative disorders, including drug resistant cancers.